

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of Yan Liu, et al

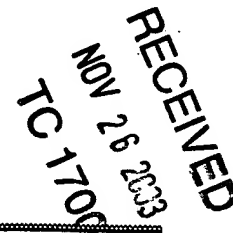
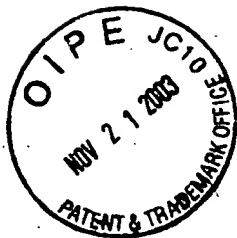
Serial No.: 09/017,050

Filing Date: 2 February 1998

For: LARGE CAPACITY ACID
OR BASE GENERATION APPARATUS
AND METHOD OF USE

Examiner: J. Ludlow

Group Art Unit: 1743



CERTIFICATE OF MAILING

I hereby certify that this correspondence, including listed enclosures, is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, DC 20231 on December 17, 1999

Signed: _____

Alison Bowden
Alison Bowden

Assistant Commissioner
for Patents
Washington, D.C. 20231

AMENDMENT

Sir:

This amendment is in response to the Official Action dated August 31, 1999.

IN THE CLAIMS

Please amend the claims as shown:

55. (Amended) The method as in one of Claims [50-54] 50, 51, 53 or 54 in which said cation source comprises a cation-containing solution selected from the group consisting of a salt solution and a cation hydroxide solution.

57. (Amended) The method of [Claims 56] Claim 52 in which said cation exchange bed comprises cation exchange resin particles in a stationary bed or suspended in an aqueous liquid.

58. (Amended) The method [as in one] of [Claims 50-54] Claim 52 in which said cation exchange bed includes a downstream weakly acidic bed section proximal to said barrier and an upstream strongly acidic bed section distal to said first barrier, said upstream and downstream sections being in fluid communication, so that the migration of hydronium ions generated at the anode through the weakly acidic bed section toward the cathode is slowed in comparison to migration of the cations.

71. The method as in one of Claims [66-70] ~~[66, 67]~~¹¹⁷ 69 or 70 in which said anion source comprises an anion-containing solution selected from the group consisting of a salt solution and an acid solution.

73. The method [as in one of Claims 66-70] ~~of Claim [68]~~¹¹⁷ in which said anion exchange bed comprises anion exchange resin particles in a stationary bed or suspended in an aqueous liquid.

74. The method [as in one of Claims 66-70] ~~of Claim [68]~~¹¹⁷ in which said anion exchange bed includes a downstream weakly basic bed section proximal to said barrier and an upstream strongly basic bed section distal to said first barrier, said upstream and downstream sections being in fluid communication, so that the migration of hydroxide ions generated at the cathode through the weakly basic bed section toward the anode is slowed in comparison to migration of the anions.

Please cancel Claims 56 and 72 without prejudice or disclaimer.

Please add the following new claims:

97. A method of generating a base comprising the steps of:

- (a) providing a cation source in a cation source reservoir,
- (b) flowing an aqueous liquid stream through a first base generation chamber separated from said cation source reservoir by a first barrier substantially preventing liquid flow while providing a cation transport bridge, said first barrier being at least one mm thick,
- (c) applying an electric potential between an anode in electrical communication with said cation source reservoir and a cathode in electrical communication with said first base generation chamber to electrolytically generate hydroxide ions in said first base generation chamber and to cause cations in said cation source reservoir to electromigrate toward said first barrier and to be transported across said first barrier toward said cathode to combine with said transported cations to form cation hydroxide, and
- (d) removing the cation hydroxide in an aqueous liquid stream as an effluent from said first base generation chamber.

98. The method of Claim 97 in which the volume of said cation source reservoir is at least about 5 times the volume of said first base generation chamber.

99. The method of Claim 97 in which said first base generation chamber is pressurized and the pressure maintained in said first base generation chamber is at least about 2 times any pressure maintained in said cation source reservoir.

100. The method of Claim 97 used to form a base eluent for an anion analysis system further comprising the steps of:

(e) flowing said cation hydroxide generated in step(d) and a liquid sample containing anions to be detected through a chromatographic separator in which anions to be detected are chromatographically separated, forming a chromatograph effluent, and

(f) flowing said chromatography effluent, with or without further treatment, past a detector in which the separated ions in said chromatography effluent are detected.

101. The method of Claim 97 in which a pressure of at least 500 psi is maintained in said first base generation chamber.

102. A method of generating an acid comprising the steps of:

(a) providing an anion source in an anion source reservoir,

(b) flowing an aqueous liquid stream through a first acid generation chamber separated from said anion source reservoir by a first barrier substantially preventing liquid flow while providing an anion transport bridge, said barrier being at least one mm thick,

(c) applying an electric potential between a cathode in electrical communication with said anion source reservoir and an anode in electrical communication with said first acid generation chamber to electrolytically generate hydronium ions in said first acid generation chamber and to cause anions in said anion source reservoir to electromigrate toward said first barrier and to be transported across said first barrier toward said anode to combine with said transported anions to form an acid, and

(d) removing the acid in an aqueous liquid stream as an effluent from said

first acid generation chamber.

103. The method of Claim 102 in which the volume of said anion source reservoir is at least about 5 times the volume of said first acid generation chamber.

104. The method of Claim 102 in which said first acid generation chamber is pressurized and the pressure maintained in said first acid generation chamber is at least about 2 times any pressure maintained in said anion source reservoir.

105. The method of Claim 102 in which a pressure of at least 500 psi is maintained in said first acid generation chamber.

106. A method of generating a base comprising the steps of:

- (a) providing a cation source in a cation source reservoir,
- (b) pumping an aqueous liquid stream through a first base generation chamber using a pump with an outlet disposed upstream of a first base generation chamber which is separated from said cation source reservoir by a first barrier substantially preventing liquid flow while providing a cation transport bridge,
- (c) applying an electric potential between an anode in electrical communication with said cation source reservoir and a cathode in electrical communication with said first base generation chamber to electrolytically generate hydroxide ions in said first base generation chamber and to cause cations in said cation source reservoir to electromigrate toward said first barrier and to be transported across said first barrier toward said cathode to combine with said transported cations to form cation hydroxide, and

(d) removing the cation hydroxide in an aqueous liquid stream as an effluent from said first base generation chamber.

107. The method of Claim 106 in which said first base generation chamber is pressurized by said pump and the pressure maintained in said first base generation chamber is at least about 2 times any pressure maintained in said cation source reservoir.

108. The method of Claim 106 used to form a base eluent for an anion analysis system further comprising the steps of:

(e) flowing said cation hydroxide generated in step(d) and a liquid sample containing anions to be detected through a chromatographic separator in which anions to be detected are chromatographically separated, forming a chromatograph effluent, and

(f) flowing said chromatography effluent, with or without further treatment, past a detector in which the separated ions in said chromatography effluent are detected.

109. The method of Claim 106 further comprising, prior to step (e) the following step:

(g) pumping through a gradient pump one or more gradient eluents into said cation hydroxide eluent stream.

110. A method of generating an acid comprising the steps of:

(a) providing an anion source in an anion source reservoir,

(b) pumping an aqueous liquid stream through a first acid generation chamber using a pump with an outlet disposed upstream of a first acid generation chamber which is separated from said anion source reservoir by a first barrier substantially preventing liquid flow while providing an anion transport bridge,

(c) applying an electric potential between a cathode in electrical communication with said anion source reservoir and an anode in electrical communication with said first acid generation chamber to electrolytically generate hydronium ions in said first acid generation chamber and to cause anions in said anion source reservoir to electromigrate toward said first barrier and to be transported across said first barrier toward said anode to combine with said transported anions to form an acid, and

(d) removing the acid in an aqueous liquid stream as an effluent from said first acid generation chamber.

111. The method of Claim 109 in which said first acid generation chamber is pressurized by said pump and the pressure maintained in said first acid generation chamber is at least about 2 times any pressure maintained in said anion source reservoir.

112. The method of Claim 110 used to form an acid eluent for an cation analysis system further comprising the steps of:

(e) flowing said acid generated in step(d) and a liquid sample containing cations to be detected through a chromatographic separator in which cations to be detected are chromatographically separated, forming a chromatography effluent, and

(f) flowing said chromatography effluent, with or without further treatment,

past a detector in which the separated cations in said chromatography effluent are detected.

REMARKS

Referring to paragraph 4 of the office action, Claims 50, 52, 53, 55-64, 66, 68, 69 and 71-80 are rejected under 35 U.S.C. §103(a) as being unpatentable over Dasgupta et al '204.

The disclosure of Dasgupta is primarily directed to a method for generating a high purity eluent from a low purity one (e.g. NaOH) and for controlling the concentration of the eluent for use in chromatography. Referring to Figure 1, a sodium hydroxide solution from source 23 flows in a stream through a source channel on one side of a permeable membrane. An aqueous liquid such as water flows in a product channel on the other side of the membrane. When an electrical potential is applied across the membrane, sodium ions pass through the membrane into a water stream in the product channel which has been electrolyzed to reform sodium hydroxide for passage from the product channel to a pump for use as the eluent for chromatography. The examiner concedes that Dasgupta fails to explicitly teach the claimed volume ratio, an ion exchange bed or a non-flowing reservoir.

Claim 50 recites a volume ratio of the cation source reservoir to the first base generation chamber of at least about five times. The importance of this ratio is that it defines a large volume cation source reservoir compared to the base generation chamber to provide a long term supply of cations. As set forth in the accompanying Liu declaration, this permits long term usage of a large capacity acid or base generation apparatus. This contributes to the commercial success of a product introduced by Dionex in 1998 under the trademark EG40 Eluent Generator.. The total revenue of EG40 products between April 1, 1998 and December 10, 1999 is

about \$4.95 million. See paragraph 3 of the accompanying declaration of Dr. Yan Liu ("the Liu Declaration").

In contrast, Dasgupta only discloses a continuous flow of a source of cations, preferably a cation hydroxide such as sodium hydroxide. This requires the use of separate pumps for the cation hydroxide and for the chromatographic system. In contrast, the present system can operate with a single chromatographic pump which directs flow of the aqueous liquid stream through the base generation chamber and then to the chromatographic column. Dasgupta experimented with a large number of different configurations as illustrated in the Dasgupta patent and in a paper by the inventors of the Dasgupta patent describing the system entitled "Electrodialytic Eluent Production in Gradient Generation in Ion Chromatography" (*Anal Chem.* 1991, 63, 480-486 (copy enclosed as Exhibit A). At the bottom of the second column of page 481, the Dasgupta inventors stated "Over 50 generators representing over a dozen designs were investigated . . .". Yet the present system using a static large capacity reservoir was not one of the many different designs set forth in the publication or in the Dasgupta '024 patent. The advantages of using a large static reservoir without a pump is neither disclosed nor suggested by Dasgupta.

Referring to Claim 51, the pressure maintained in the first base generation chamber is at least about two times any pressure maintained in the cation source reservoir. This reflects the operation of the present system using the high pressure chromatographic pump for the aqueous liquid stream flowing through the base generation chamber in contrast to the cation source reservoir which can be maintained at atmospheric pressure.

In contrast, Dasgupta does not teach any difference in pressure between the channels. Moreover, it discloses pump 22 which is downstream of the eluent

generator, requiring a separate pump for the cation source solution. Also, Dasgupta teaches away from the use of high pressure in the base generator because of the setup and because of the disclosed thin membranes. See column 6, lines 32-49. The actual membrane separators used in the Dasgupta examples have thicknesses in the range of 2-4 mil (thousandths of an inch) and a maximum disclosed membrane thickness of 10 mil. (10 mil is 0.254 mm.) (Liu Declaration, ¶ 4) Converting to the metric system, the actual thickness of the membrane used in Dasgupta are about of 0.05 to 0.1 mm and the maximum disclosed thickness is about 0.25 mm. The thin membrane and the device disclosed in Dasgupta are the same as in the membrane suppressor disclosed in Pohl, U.S. Patent No. 4,999,098. That patent used such thin membranes which permits rapid ion transport in a flowing stream for use as a suppressor. As illustrated at paragraph 7 of the Liu Declaration, experiments have been performed showing that eluent generator devices built with membranes of 0.86 mm in thickness (over three times the maximum thickness disclosed in Dasgupta) could leak at 1,000 psi of pressure.

Referring to Claim 52, the cation source is specified to comprise a cation exchange bed including exchangeable cations of the type which form a cation hydroxide. The examiner points to Dasgupta column 5, lines 26-30 regarding disclose ion exchange screens or particles in the source channel. However, in the next paragraph (column 5, lines 31-45) the purpose of the screen is specified as providing ion paths of the type described in EPA 180321, the same as U.S. Patent No. 4,999,098. The screens or particles are not disclosed as the source of ion particles but as conductivity paths for the ion which are provided from another flowing source of cations. (Liu Declaration, ¶ 5)

In contrast to the Dasgupta '204 patent, Claim 52 specifies that the cation

source is a cation exchange bed. This is neither disclosed nor suggested by Dasgupta which instead discloses the cation source to be a continuously flowing cation hydroxide solution. As set forth in ¶ 5 of the Liu Declaration, this approach eliminates Donnan leakage compared to the continuously flowing solutions.

Referring to Claim 53, the cation source reservoir contains substantially non-flowing aqueous liquid. As set forth above, a normally static reservoir of large volume provides a long term supply of cations without the necessity of a continuously flowing stream of a cation source, sodium hydroxide. The static reservoir can be replaced on depletion by emptying the container and replacing it with a fresh cation source. This approach is not suggested in Dasgupta in spite of the many different models considered by Dasgupta as set forth in his enclosed paper.

Referring to Claim 54, Dasgupta does not suggest a cation source reservoir which is replenished by recycling an aqueous liquid stream. This type of approach can be used intermittently.

Referring to Claim 58, the specific form of cation exchange bed including a downstream weakly acid bed section proximal to the barrier and an upstream strongly acidic section distal to the barrier is neither disclosed nor suggested by the prior art. This arrangement provides the advantage of slowing the migration of the hydronium ions in comparison to the cations.

Claims 66-81 are mirror images of Claims 50-65 for generating an acid instead of a base. The above arguments apply with equal force to these claims.

New Claim 97 specifies that the first barrier is at least 1 mm thick. Support of this claim found at page 8, lines 7 and 8 of the present specification. In contrast, the preferable membrane thickness and the ones used in the examples of Dasgupta are

between 0.05 and 0.1 mm in thickness with a maximum disclosed size of 0.25 mm thick, one-fourth the minimum thickness set forth in Claim 97. Thicknesses of 0.86 mm can leak at pressures as low as 1,000 psi. Membranes of 1-3 mm thickness are described in the present specification (page 8, lines 3-8) to have sufficient thickness to withstand pressures on the order of 1,000-3,000 psi.

Moreover, the use of the thin membrane barriers of Dasgupta could create serious Donnan leakage particularly for use of a salt as the cation source. The anion component of the salt tends to leak through a membrane as thin as disclosed in the Dasgupta patent, which can seriously interfere with the analysis. (Liu Declaration, ¶¶ 5 and 10.)

Claim 99 recites that the pressure in the base generation chamber is a least two times the pressure in the cation source reservoir. Claim 101 (support p. 11, lines 20-22 of the specification) recites that the pressure maintained in the first base generation chamber is at least 500 psi. In Dr. Liu's opinion, the thin membranes disclosed in Dasgupta tend to rupture or leak at such pressures. These claims, neither disclosed nor suggested in Dasgupta, illustrate features of the present invention in a system in which the pumping pressures can be adequate for liquid chromatography as in Claim 100.

Claim 106 recites that the aqueous liquid stream is pumped through the first base generation chamber using a pump with an outlet disposed upstream of the base generation chamber. Thus, the aqueous liquid stream through the base generator and through chromatography column are pumped by a single pump upstream of the base generator. The advantages of this setup are multi-fold. For example, water, rather than generated acid or base, flows through the pump. Thus, the lifetime of the pump is significantly improved over a pump which must pass corrosive acid or

base. Moreover, the pump has a dead volume which can create error particularly for the use of gradient eluents. This source of error is eliminated by the method of Claim 106 in which the pump is upstream of the eluent generator. (Liu Declaration, ¶ 10).

Referring to paragraph 5, Claims 51, 54-65, 66, 70-81 are rejected as being unpatentable over Dasgupta as applied to Claims 50, 52-53, 54-55-64, 66, 68, 69 and 71-80 above, and further in view of Anderson Jr et al. ,

Anderson teaches electrolytic eluent generation in a packed bed. There is no barrier separating the packed bed from another chamber in which the acid or base is generated or of applying an electrical potential between two chambers. It does not solve the deficiencies of Dasgupta in that it is a different approach to generation which does address the differential pressure on either side of the barrier as set forth above. Since the invention of the present application revolves around use of such a barrier to separate a source chamber from an acid or base generation chamber, Anderson's disclosure of generation in a packed bed is not relevant to the present claims. It is submitted that the technologies are so different that the references are not properly combinable.

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,

FLEHR HOHBACH TEST
ALBRITTON & HERBERT LLP

Date: December 17, 1999



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EXAMINER

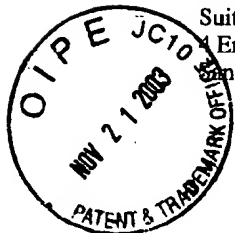
LUDLOW, JAN M

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EXAMINER

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Commissioner for Patents

Jan M. Ludlow
Primary Examiner
Art Unit: 1743

Art Unit: 1743

1. The reply filed on July 31, 2003 is not fully responsive to the prior Office Action because of the following omission(s) or matter(s): The response makes reference to Exhibit A, but Exhibit A is not present in the file. See 37 CFR 1.111. Since the above-mentioned reply appears to be *bona fide*, applicant is given **ONE (1) MONTH or THIRTY (30) DAYS** from the mailing date of this notice, whichever is longer, within which to supply the omission or correction in order to avoid abandonment.

EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jan M. Ludlow whose telephone number is (703) 308-4039. The examiner can normally be reached on Monday-Thursday, 11:30 am - 8:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (703) 308-4037. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.



Jan M. Ludlow
Primary Examiner
Art Unit 1743

Jml
October 20, 2003